ABSTRACT

Borrelia burgdorferi is a spirochetal bacterium that causes Lyme disease, which is the most prevalent tick-borne disease in North American and Eurasia. Notable, this pathogen displays unique endoflagellar motility to efficiently disseminate through dense host tissues, and eventually persist within target tissues to cause inflammation-associated disease. Unfortunately, the importance of different *B. burgdorferi* virulence mechanisms, particularly those involved in bacterial motility/chemotaxis, cannot be accurately assessed *in vitro* since the complexity of the host tissues cannot be appropriately replicated for this obligate parasite. Hence, our initial goal was to develop intravital microscopy techniques that allow direct observation of fluorescent *B. burgdorferi* within the intact ear skin of living mice, including distinguishing specific motility parameters and *B. burgdorferi*-interactions with host immune cells. Our analyses determined that *B. burgdorferi* injected into murine skin undergo massive proliferation between Days 3-5, followed by a rapid decrease to a stable low level by Day 12; these levels are m

ction s due to clearance
sus t ctivities mediated
at re significant levels
r, ou ravital techniques
llent del for accurately
anism *n vivo*.

rmin the relative im-
hemo is for evasion of
muta that lacked either
ellar tion; Δ*motB*) and
; Δ*ch*), respectively. *In*
here he Δ*cheY3* mutant
Δ*mo* *B. burgdorferi* did
l sha as motor rotation
ellar bon, as shown by
n-mo and was cleared
on. *vivo*, Δ

cheY3 B. burgdorferi retained the spirochetal shape but not the motility pattern of wild-type (WT) *B. burgdorferi*; the mutants displayed rapid velocities, but were unable to reverse directions and were cleared from all tissues by Day 5 post-injection. Interestingly, Δ*motB*-infection elicited very few *B. burgdorferi*-specific antibodies, whereas Δ*cheY3* elicited similar *B. burgdorferi*-specific antibody levels as WT through 28-days post-injection, but did not increase further compared to WT *B. burgdorferi* infection. Notably, the complexity of antigens recognized by Δ*cheY3*-elicited antibodies was less than WT, but contained antibodies against many proteins expressed by WT *B. burgdorferi in vivo*. These findings suggest that both *motB* and *cheY3* are essential for *B. burgdorferi* persistence, and that *æcheY3 B. burgdorferi* may serve as a vaccine to protect against Lyme disease.

DISSERTATION COMMITTEE

R Mark Wooten, Ph.D., Major Advisor

Robert Blumenthal, Ph.D.

Andrea Kalinoski, Ph.D.

Stanislaw Stepkowski, D.V.M., PH.D., D.SC.

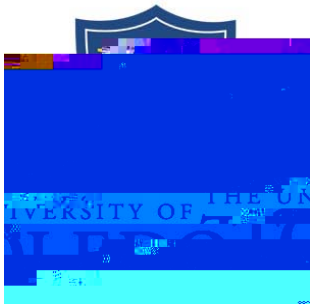
Akira Takashima, M.D., Ph.D.

Kandace J. Williams, Ph.D., Graduate School Representative

The University of Toledo College of Medicine and Life Sciences

Infection, Immunity & Transplantation (IIT) Track

Department of Medical Microbiology & Immunology



DISSERTATION PRESENTATION

Padmapriya Sekar

April 30, 2015

The effects of key motility and chemotaxis genes for *Borrelia burgdorferi* dissemination and evasion of immune clearance in murine tissues

Ph.D. in

Biomedical Sciences

Sultan SZ, Sekar P, Zhao X, Manne A, Liu J, Wooten RM, Motaleb MA Motor rotation is essential for the formation of the periplasmic flagellar ribbon, cellular morphology, and *Borrelia burgdorferi* persistence within *Ixodes* tick and murine hosts. Infect Immun. 2015 May; 83(5):1765-77

J. P. Lavik,* P. Sekar,* V. Shukla, A. L. Nestor-Kalinoski, and R. M. Wooten. Intravital imaging in murine skin reveals that *Borrelia burgdorferi*